

REMARKS

Status of the Claims

Claims 1-15 and 17-33 are pending in the current application. Reexamination and reconsideration are respectfully requested.

Consideration Of Previously Submitted Information Disclosure Statement

It is noted that an initialed copy of the PTO Form 1449 that was submitted with Applicants' Information Disclosure Statement filed April 27, 1999 has not been returned to Applicants' representative with the Office Action. Accordingly, it is requested that an initialed copy of the Form 1449 be forwarded to the undersigned with the next communication from the PTO. In order to facilitate review of the references by the Examiner, a copy of the Information Disclosure Statement and the Form 1449 are attached hereto. Copies of the cited references were provided at the time of filing the original Information Disclosure Statement, and, therefore, no additional copies of the references are submitted herewith. Applicants will be pleased to provide additional copies of the references upon the Examiner's request if it proves difficult to locate the original references.

The Rejection Under 35 U.S.C. § 103(a) Should be Withdrawn:

The Examiner has withdrawn the rejection of claims 1-15 and 17-23. However, the rejection of claims 24 and 25 under 35 U.S.C. § 103(a) has been maintained on the grounds that these claims are unpatentable over NCBI Accession No. AJ222589 in view of Ikejima *et al.* (1990) *J. Biol. Chem.* 265:21907-13. The rejection is respectfully traversed for the reasons described below.

NCBI Accession No. AJ222589 discloses a nucleotide sequence that has approximately 97% sequence identity with the nucleotide sequence set forth in SEQ ID NO:1 and encodes a protein having approximately 95% sequence identity with the amino acid sequence set forth in SEQ ID NO:2. The protein encoded by NCBI Accession No. AJ222589 lacks amino acids 54-64 of SEQ ID NO:2. Amino acids 54 and 55 of SEQ ID NO:2 lie within the first of the two zinc

finger domains found in this protein, and amino acid 55 is a cysteine known to be required for the coordination of zinc by the zinc finger domain.

Ikejima *et al.* (1990) *J. Biol. Chem.* 265:21907-13 teach that variants of human poly(ADP-ribose) polymerase that contain mutations or deletions in the first of the two zinc fingers found in wild type human poly(ADP-ribose) are not activated by damaged DNA.

Claim 24 is drawn to an isolated DNA molecule comprising a nucleotide sequence having at least 90% sequence identity to SEQ ID NO:1, wherein said nucleotide sequence encodes a polypeptide having poly ADP-ribose activity and comprising at least two functional zinc fingers. Claim 25 is drawn to the DNA molecule of claim 24, wherein the nucleotide sequence comprises the sequence set forth in SEQ ID NO:5.

The Examiner argues that although the sequence of NCBI Accession No. AJ222589 does not contain two functional zinc fingers, it would be obvious to modify this sequence to contain two zinc fingers in view of the teachings of the Ikejima *et al.* reference and therefore the DNA molecules recited in claims 24 and 25 are obvious under 35 U.S.C. § 103(a).

As noted in Applicant's Amendment mailed December 11, 2002, the Federal Circuit held in *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991) that:

Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed compositions or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making and carrying out, those of ordinary skill would have a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be found in the prior art, not in the applicant's disclosure.

In re Vaeck at 1442, citing *In re Dow Chemical Co.*, 5 USPQ2d 1459, 1531 (Fed. Cir. 1988). Furthermore, to establish *prima facie* obviousness of a claimed invention, all of the claim limitations must be taught or suggested by the prior art. *Manual of Patent Examining Procedure* § 2143.03 (8th ed.), citing *In re Royka*, 180 USPQ 580 (CCPA 1974). In the present case, no *prima facie* case of obviousness has been established for the invention of claims 24 and 25

because the cited references do not provide a motivation or suggestion to those of ordinary skill in the art to modify the nucleotide sequence disclosed in NCBI Accession No. AJ222589 to produce a DNA molecule comprising a nucleotide sequence having at least 90% sequence identity to SEQ ID NO:1, where the nucleotide sequence encodes a polypeptide having at least two functional zinc fingers. The suggestion to combine the references to make the claimed invention must be found in the prior art, not in the applicant's disclosure. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *Manual of Patent Examining Procedure* § 2143.01 (8th ed.), citing *In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990).

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The gene report for NCBI Accession No. AJ222589 does not teach or suggest that the protein encoded by this nucleotide sequence contains a non-functional zinc finger domain, or that the disclosed nucleotide sequence could or should be modified to encode a protein having two functional zinc fingers. Ikejima *et al.* teach that two functional zinc fingers are required for the enzymatic activity of human poly(ADP-ribose) polymerase, but do not teach or suggest the desirability of modifying other poly(ADP-ribose) polymerase-related proteins to produce at least two functional zinc fingers. The Examiner argues that because Ikejima demonstrate that both zinc fingers are required for the function of human poly(ADP-ribose), this reference "implicitly teaches one of skill in the art to provide for two functional zinc finger domains in order to provide a protein with enzymatic activity." February 26, 2003 Office Action, page 3.

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In fact, the two references taken together do not provide the motivation or suggestion to modify the sequence of NCBI Accession No. AJ222589 such that it contains two functional zinc finger domains because 1) the references, alone or in combination, do not teach that the sequence of NCBI Accession No. AJ222589 contains an incomplete zinc finger domain; 2) the references, alone or in combination, do not teach that the maize protein encoded by NCBI Accession No. AJ222589 is not enzymatically active; and 3) the references, alone or in combination, do not teach that the insertion of amino acids following residue 53 of the protein encoded by NCBI Accession No. AJ222589 are required to render this protein enzymatically active.

The Examiner's argument appears to be based on the premise that Ikejima *et al.* provide an implicit suggestion to those of skill in the art that *any* protein that shares sequence identity

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implicit

with human poly(ADP-ribose) but does not contain two zinc fingers should be modified to contain two zinc fingers. However, Ikejima *et al.* do not explicitly or implicitly suggest that because human poly(ADP-ribose) requires two zinc fingers for enzymatic activity, all proteins having homology to human poly(ADP-ribose) will require two zinc fingers and should, if necessary, be modified accordingly. In determining the motivation provided to one of skill in the art to modify the sequence shown in NCBI Accession Number AJ222589, it is important to recognize that the disclosed sequence is described by the authors of this gene record as being a *native* maize sequence, not a maize mutein. One of skill in the art would not be motivated to modify a *native* sequence to give it enzymatic activity, because one of skill in the art would believe that a sequence described as being found naturally in maize would already have enzymatic activity.

In addition, the sequence studied in the Ikejima *et al.* reference is a human sequence, while the sequence disclosed in NCBI Accession No. AJ222589 is a maize sequence. In view of the wide divergence between human and maize, and the low degree of sequence similarity between the protein encoded by Accession No. AJ222589 and the protein studied by Ikejima *et al.*, one of skill of art would not be motivated to modify the maize sequence to contain two functional zinc fingers based on the fact that the human sequence contained two functional zinc fingers.

Finally, even if the AJ222589 gene record taught that the disclosed sequence contained one functional zinc finger domain (and it does not), one of skill in the art would not be motivated to modify the sequence to produce a second zinc finger domain, because enzymatically active proteins having only one zinc finger domain, including some proteins having sequence similarity to human poly(ADP-ribose) polymerase, are known to those of skill in the art. See, for example, Wei *et al.* (1995) *Molec. Cell. Biol.* 15:3206-18, a copy of which is provided as Appendix A for the convenience of the Examiner. Wei *et al.* describe the cloning of a cDNA encoding human DNA ligase III. This reference shows that the encoded protein has a single zinc finger domain (see the figure legend for Figure 5), that human DNA ligase III shares sequence similarity with human PARP (see Figure 7 and column 1 on page 3213), and that human DNA ligase III is enzymatically active (see Figure 4).

Furthermore, Applicants note that patent publication WO 00/04173 which was published subsequent to the filing date of the present application, teaches that an *Arabidopsis* sequence, APP, and a maize sequence, NPP encode PARP proteins that are functional even though they have only a single zinc finger. See, for example, the sentence beginning on the last line of page 17 of the WO 00/04173 application (provided herewith for the convenience of the Examiner as Appendix B), which states "[t]hat the second class of PARP proteins are indeed functional PARP protein, i.e. are capable of catalyzing DNA dependent poly(ADP-ribose) polymerization has been demonstrated by the inventors." Accordingly, *Arabidopsis* and maize homologs of the sequence encoded by AJ222589 have been shown to be functional active PARP proteins in the absence of modification to introduce a second zinc finger.

Thus, considered together, the cited references would not have provided one of skill in that art with an explicit or implicit suggestion that it would be desirable to modify the maize sequence disclosed in AJ222589 such that it encoded a protein having two functional zinc fingers because one of skill in the art would believe that a native maize sequence encoded a protein that was enzymatically active in the absence of modification, because the species that are the source of the sequences described in the references are highly divergent, and because enzymatically active proteins having sequence similarity with human poly(ADP-ribose) polymerase and containing a single zinc finger domain were known in the art. Accordingly, the combination of references does not motivate one of skill in the art to make the invention of claims 24 and 25, because they do not suggest a DNA molecule comprising a nucleotide sequence having at least 90% sequence identity to SEQ ID NO:1, wherein said nucleotide sequence encodes a polypeptide having poly ADP-ribose activity and *comprising at least two functional zinc fingers*.

35 U.S.C. § 103(a) provides that claims must not be rejected for obviousness unless "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time that the invention was made." At the time the present invention was made, the prior art did not provide a motivation to modify the nucleotide sequence of NCBI Accession No. AJ222589 to encode a protein having two functional zinc fingers. Rather, it is the Applicant's disclosure that provides the motivation to

make such a modification. Accordingly, the requirements for a *prima facie* case of obviousness have not been met for claims 24 and 25.

The rejection of claims 26-33 under 35 U.S.C. § 103(a) as being unpatentable over NCBI Accession No. AJ222589 and Ikejima *et al.* in further view of WO 97/06267 has been maintained. The rejection is respectfully traversed for the reasons described below.

WO 97/06267 teaches a method of producing transgenic plant cells, comprising the steps of culturing untransformed cells with an inhibitor of poly(ADP-ribose) polymerase activity for a period of time sufficient to reduce the response of the cultured cells to stress and reduce their metabolism, and then contacting the cells with a foreign DNA of interest. This international patent application demonstrates that pre-treatment of the untransformed cells with inhibitors of poly(ADP-ribose)polymerase increases transformation efficiency. The Examiner argues that in view of the disclosure of WO 97/06267, it would be obvious to modify the sequence of NCBI Accession No. AJ222589 to produce a sequence having two functional zinc fingers, and then use this sequence to modulate plant metabolism.

The combination of references cited in the Office Action does not establish a *prima facie* case of obviousness for the compositions and methods of claims 26-33. As described above, the DNA molecules of claims 24 and 25 are not obvious in view of NCBI Accession No. AJ222589 and Ikejima *et al.* Therefore, the DNA constructs, transformed plant cells, transformed plants, and seeds containing these non-obvious DNA molecules as recited in claims 26-32, and the methods of using these non-obvious DNA molecules as recited in claim 33 are necessarily non-obvious. Because there was no suggestion or motivation to one of ordinary skill in the art to prepare the nucleic acid molecules recited claims 24 and 25, there could be no motivation or suggestion to use these nonobvious DNA molecules to produce DNA constructs, transformed plant cells, transformed plants, and seeds, and no motivation or suggestion to use the nonobvious DNA molecules in a method of modulating the metabolic state of a plant cell.

In re: Mahajan et al.
Appl. No. 09/236,995
Filed: January 26, 1999
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In view of the above arguments, all grounds for rejection under 35 U.S.C. § 103 have been overcome. Accordingly, reconsideration and withdrawal of the rejections are respectfully requested.

CONCLUSIONS

It is believed that all the rejections have been obviated or overcome and the claims are in conditions for allowance. Early notice to this effect is solicited.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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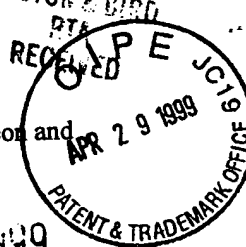
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Date Mailed: 04/27/99
Atty. Dkt. No. 5718-34

Application No. 09/236,995; Filing Date 01/26/99
Inventor(s): Mahajan et al.; Title of Invention: POLY ADP-RIBOSE
POLYMERASE GENE AND ITS USES
Documents Enclosed: Information Disclosure Statement 1 page / Form 1449 -
2 pages / 11 supporting attachments

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